Safety Data Sheet

Arsenic and compounds

Division of Safety
National Institutes
of Health

WARNING!

COMPOUNDS IN THIS CLASS ARE ACUTELY TOXIC, CARCINOGENIC, TERATOGENIC, AND MUTAGENIC. THEY ARE READILY ABSORBED BY VARIOUS BODY TISSUES THROUGH THE SKIN, RESPIRATORY AND INTESTINAL TRACTS, AND TRANSPLACENTALLY. THEY MAY CAUSE SEVERE IRRITATION OF TISSUES (SKIN, EYES, MUCOUS MEMBRANES, AND LUNGS). AVOID FORMATION AND BREATHING OF AEROSOLS OR VAPORS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH DILUTE BORIC ACID SOLUTION FOLLOWED BY WATER. AVOID RUBBING OF SKIN OR INCREASING ITS TEMPERATURE.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH DILUTE BORIC ACID SOLUTION FOLLOWED BY LARGE AMOUNTS OF WATER. FOR INGESTION, INDUCE VOMITING. REFER FOR GASTRIC LAVAGE. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. AVOID SKIN CONTACT OR BREATHING OF AEROSOLS OR VAPORS. USE DILUTE NITRIC ACID SOLUTION TO DISSOLVE ARSENIC METAL, AND DILUTE HYDROCHLORIC ACID FOR OTHER ARSENIC COMPOUNDS. USE ABSORBENT PAPER TO MOP UP SPILL. WASH DOWN AREA WITH SOAP AND WATER. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY. MONITOR LABORATORY AIR AND CHECK FOR ARSENIC RESIDUES AFTER CLEAN-UP.

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Prepared by the Environmental
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A. Background

Elementary arsenic is a gray metallic-looking crystalline powder; arsine is a colorless gas; arsenites and arsenates are white crystalline powders. The alkali salts are highly soluble in water but the calcium and lead salts are not.

All arsenic compounds are moderately toxic (arsine is highly toxic), mutagenic in some but not all test systems, and teratogenic. With regard to carcinogenicity, IARC (1980) states that "there is inadequate evidence for the carcinogenicity of arsenic compounds in animals. There is sufficient evidence that inorganic arsenic compounds are skin and lung carcinogens in humans." Since that time several investigations have demonstrated carcinogenicity in several animal species also.

Major uses of arsenic in various forms are as pesticides (insecticides, herbicides, and sheep and cattle dips) and in drugs. The use of "Fowler's solution" (potassium arsenite) in the treatment of psoriasis has been almost entirely discontinued.

Arsenic may be found in any of four valence states: -3 (arsine), 0 (elementary arsenic), +3 (arsenites), and +5 (arsenates). Nearly all experimental work on arsenites and arsenates has been carried out on their sodium or potassium salts, and most of the pertinent physical and chemical properties are listed for these salts. The term "arsenic" is used when the valence state is not specified and generally refers to arsenite and/or arsenate.

The current permissible exposure limit at work places has been established at 0.2 mg/m^3 for arsenic, its soluble compounds (as As), and arsine, averaged over an 8-hour period (ACGIH, 1987). The latest 8-hour time-weighted average is 0.15 mg/m^3 for lead arsenate (ACGIH, 1987). For a review of the development of these limits, see Sittig (1985).

Recent reviews of the chemical and biological properties of arsenic compounds include Landrigan (1981); Fowler (1983); Lederer and Fensterheim (1983); Sunderman (1984); and IARC (1986).

B. Chemical and Physical Properties

For properties not listed under individual entries, see the end of this section.

Arsenic

1. Chemical Abstract No.: 7440-38-2

2. Synonyms:

Gray arsenic	Metallic arsenic

3. Chemical formula: As; atomic weight: 74.92

4. Density: 5.727 g/cm^3 at 20°C relative to water at 4°C.

5. Solubility: Insoluble in water; soluble in nitric acid to form arsenious and arsenic acids.

6. Description: Gray, shiny, metallic-looking rhombohedra.

7. Boiling point: 613°C (sublimes).

   Melting point: 817°C at 28 atmospheres.

8. Stability: High in the absence of oxidizers or reducers.

9. Chemical reactivity: Forms arsine (highly toxic) in the presence of nascent hydrogen.

Arsenic pentoxide

1. Chemical Abstract No.: 1303-28-2

2. Synonyms:

   Arsenic acid anhydride Arsenic [V] oxide

   Arsenic oxide [As_2O_5] (9CI)

3. Chemical formula: As_2O_5; molecular weight: 229.84

4. Density: 4.32 g/cm^3.

5. Solubility: Highly soluble in water (150 g/100 ml at 16°C), ethanol, dilute mineral acids, and alkali hydroxides.

6. Description: Deliquescent white powder.

7. Melting point: 315°C with decomposition.

8. Stability: Deliquesces in moist air to form arsenic acid. Decomposes on heating above 300°C to As_2O_3 and O_2.

9. Chemical reactivity: Acts as an oxidant in acid solution.

Arsenic trioxide

1. Chemical Abstract No.: 1327-53-3

2. Synonyms:

Arsenic (III) oxide	Arsenous acid
Arsenic sesquioxide	White arsenic
Arsenous oxide	Arsenous acid anhydride
Arsenic oxide (As_2O_3) (9CI)	

3. Chemical formula: As_2O_3; molecular weight: 197.84

4. Density: 3.738 g/cm^3.

5. Volatility: 1 mm Hg at 212.5°C. (For other values, see Weast 1979, p. D-199.)

6. Solubility: 3.7 g/100 ml at 20°C in water;[A] soluble in HCl, alkali hydroxides; practically insoluble in ethanol or ether.

7. Description: Amorphous or crystalline (claudetite, arsenolite) powder.

8. Melting point: 312.3°C;[A] sublimes if heated slowly.

9. Stability: Stable to heat and light.

10. Chemical reactivity: Reduced to arsenic by heating with charcoal or in HCl solution by stannous chloride; reduced to arsine by nascent hydrogen (Zn + HCl); oxidized to arsenate by various oxidants in alkaline solution.

Arsine

1. Chemical Abstract No.: 7784-42-1

2. Synonyms:

Arsenic hydride	Hydrogen arsenide

3. Chemical formula: AsH_3; molecular weight: 77.95

4. Density: 2.695 as a gas (air=1).

5. Volatility: 1 mm Hg at -142.6°C. (For other values, see Weast 1979, p. D-199.)

6. Solubility: Slightly soluble in water (20 ml/100 ml); soluble in chloroform and benzene.

7. Description: Colorless gas.

[A] These values are for the amorphous forms. Those for the crystalline forms are listed in Weast (1979), p. B-57.

8. Boiling point: -55°C.

   Melting point: -116.3°C.

9. Stability: Decomposes on heating below 300°C to arsenic and hydrogen. Decomposition is accelerated by light in the presence of moisture. Stable in air at room temperature but ignitable to yield arsenic, arsenic trioxide, or arsenic pentoxide (depending on oxygen supply).

10. Chemical reactivity: Oxidized by oxidants (permanganate, bromine water); reduces silver nitrate solutions to metallic silver.

Calcium arsenate

1. Chemical Abstract No.: 7778-44-1

2. Synonyms:

   Tricalcium arsenate Pencal

   Arsenic acid [H_3AsO_4], calcium salt (2:3) (9CI)

3. Chemical formula: $Ca_3(AsO_4)_2$; molecular weight: 398.08

Lead arsenate

1. Chemical Abstract No.: 7784-40-9

2. Synonyms:

   Arsenic acid [H_3AsO_4], lead(2+) salt (1:1) (9CI)

   Acid lead arsenate Schultenite

   Lead di-ortho-arsenate

3. Chemical formula: $PbHAsO_4$; molecular weight: 347.12

4. Solubility: Very slightly soluble in water; soluble in nitric acid, alkali.

Potassium arsenate[A]

1. Chemical Abstract No.: 7784-41-0

[A]Other forms are listed in Weast (1979).

2. Synonyms:

Arsenic acid [H_3AsO_4], monopotassium salt (9CI)

Potassium dihydrogen arsenate Macquer's salt

3. Chemical formula: KH_2AsO_4; molecular weight: 180.04

Potassium arsenite[A]

1. Chemical Abstract No.: 13464-35-2

2. Synonyms:

Arsenous acid, potassium salt (9CI)

Potassium metaarsenite

3. Chemical formula: $KH(AsO_2)_2$; molecular weight: 253.93

Note: "Fowler's solution" is a 1% aqueous solution of $KH(AsO_2)_2$.

Sodium arsenate (heptahydrate)[A]

1. Chemical Abstract No.: 10048-95-0

2. Synonyms:

Dibasic sodium arsenate heptahydrate

Sodium orthoarsenate, mono H, heptahydrate

Arsenic acid (H_3AsO_4), disodium salt, heptahydrate (9CI)

3. Chemical formula: $Na_2HAsO_4 \cdot 7H_2O$); molecular weight: 311.9

4. Stability: Loses 5 molecules of water at 50°C; becomes anhydrous at 100°C. Converted to sodium pyroarsenate ($Na_4As_2O_7$) at 150°C or above. A decahydrate is also known.

Sodium arsenite

1. Chemical Abstract No.: 7784-46-5

2. Synonyms:

Arsenious acid, sodium salt Sodium metaarsenite

[A]Other forms are listed in Weast (1979).

3. Chemical formula: $NaAsO_2$; molecular weight: 129.91

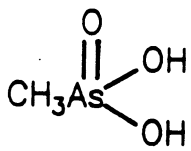
Other properties

There are no data for any of the above arsenic compounds regarding optical absorption characteristics, flash point, autoignition-temperature, or explosive limits. Alkali arsenites and arsenates are water soluble and sparingly soluble in ethanol; the calcium and lead salts are nearly insoluble in water. Arsenites and arsenates are amorphous or crystalline white powders with practically no volatility. Arsenates are stable to heat, light, and moisture (except as noted otherwise); there are no data on their chemical reactivity. Alkali arsenites are somewhat hygroscopic and decompose in the presence of atmospheric CO_2. They react with metals like aluminum and zinc to produce highly toxic arsine. Aqueous solutions of arsenites (40 or 400 µg As/ml) are stable over 4 weeks at 4°C; at room temperature, up to 40% is oxidized to arsenate in this time (Vahter and Norin, 1980).

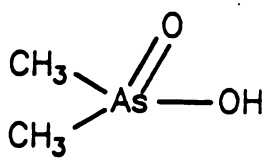
Exposure of arsenite solutions to ultraviolet light results in quantitative transformation to arsenate (Reay and Asher, 1977; Marafante et al., 1985).

Products of arsenic metabolism

Monomethylarsonic acid (MMA):



Dimethyl arsinic acid (cacodylic acid, DMA):



Fire, Explosion, and Reactivity Hazard Data

1. Fire fighters should wear a full-face-piece, self-contained breathing apparatus in positive pressure mode. While arsenic compounds are not flammable themselves, fires can produce volatile toxic products. There are no explosion hazards.

2. Conditions contributing to instability include heat and reducing materials.

3. Incompatibilities, particularly for metallic arsenic, arsenic trioxide, and alkali arsenites, are aluminum and zinc in the presence of acid.

4. Arsenic compounds do not require nonspark equipment.

Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The NIH Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving arsenic compounds.

It should be emphasized that this data sheet and the NIH Guidelines are intended as starting points for the implementation of good laboratory practices when using this compound. The practices and procedures described in the following sections pertain to the National Institutes of Health and may not be universally applicable to other institutions. Administrators and/or researchers at other institutions should modify the following items as needed to reflect their individual management system and current occupational and environmental regulations.

1. Chemical inactivation: No validated method reported.

2. Decontamination: Turn off equipment that could be affected by arsenic compounds or the materials used for cleanup. If there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 116) for assistance. Use absorbent paper to mop up spill. Wipe off surfaces with acidified water, then wash with copious quantities of water. Glassware should be rinsed in a hood with acidified water, followed by soap and water. Animal cages should be washed with water.

3. Disposal: No waste streams containing arsenic compounds shall be disposed of in sinks or general refuse. Surplus arsenic compounds or chemical waste streams contaminated with arsenic compounds shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcasses and bedding) containing arsenic compounds shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing arsenic compounds shall be disinfected by heat using a standard autoclave treatment and packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with arsenic compounds shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system. Radioactive waste containing arsenic compounds shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store solid arsenic compounds and their solutions in tightly closed glass containers. Avoid contact with container materials consisting of or containing aluminum or zinc. Avoid exposure of solid arsenic compounds to atmospheric moisture and carbon dioxide.

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

For recent reviews of sampling for analysis and analytical procedures see: Lewis (1977); Brooks et al. (1981); IARC (1986), chapters 10-12 and individual methods.

1. Sampling: Officially recommended methods for air sampling (NIOSH, 1977) are: for particulate arsenic compounds, filtration through cellulose membranes followed by ashing and solubilization in nitric acid (Procedure S-309-1-7; a portable sampling unit is described); for arsine, adsorption on charcoal and desorption with dilute nitric acid (Procedure S229-1-8). Both procedures use atomic absorption spectrometry for evaluation. A simple method for sampling and analysis of arsenic trioxide in air consists of collection on filter paper, dissolving in 1 N NaOH, and spectrometry at 222 nm (Snyder and Isola, 1979).

   Lewis (1977) cautions that significant absorption of As from biological material onto soft glass containers may lead to low analytical results; Teflon and polyethylene bottles are recommended for sample storage.

2. Analysis

   a. Total arsenic: Most methods for the analysis of water, urine, and other biological materials involve first wet ashing with nitric, sulfuric, and perchloric acid (proper control of residual acid [Kang and Valentine, 1977] and of the order of oxidizing acids [Cox, 1980] has been emphasized). Krynitsky (1987) recommends the use of nitric acid and hydrogen peroxide for wet ashing. This is usually followed by reduction with either zinc hydrochloride or sodium borohydride to arsine. In colorimetric procedures, the AsH_3 is absorbed in a pyridine solution of silver diethyldithiocarbamate to produce a red color (Burke and Diamondstone, 1977). In recent years, atomic absorption spectrometry (AAS) has become the preferred method. It has been adopted by NIOSH as the method of choice for the analysis of air and urine and these methods have been described in detail (IARC, 1986). AAS is usually preceded by graphite furnace combustion and arsine generation. Addition of EDTA to the sample mixture prevents interference from copper, iron, and nickel (Uthus et al., 1981). The advantages and disadvantages of AAS in comparison with neutron-activation-Y spectrometry, molecular absorption spectrometry, atomic emission spectrometry, electrometric methods, x-ray emission, and atomic fluorescence spectrometry have been discussed critically (Brooks et al., 1981; Maitani et al., 1987).

   b. Arsenic speciation: Differential determination of arsenite, arsenate, and organoarsenic compounds usually uses AAS preceded

by high pressure liquid chromatography. Some applications to environmental samples have been described (Ricci et al., 1981; Aggett and Kadwani, 1983; IARC, 1986; Chana and Smith, 1987). HPLC coupled with atomic emission spectrometry is stated to have a twenty-fold higher sensitivity (Morita et al., 1981) but employs a far more expensive spectrometer.

iological Effects (Animal and Human)

. Absorption: Arsenites and arsenates are absorbed by ingestion and parenteral injection; sodium arsenite, arsenic trioxide, and arsine are absorbed by inhalation. Skin absorption of arsenates, while slight, has been demonstrated and may be considered to be significant for arsine (though there is no documentation). Sodium arsenite and arsenate are absorbed through the placenta.

. Distribution and pharmacokinetics: Injected arsenites and arsenates are first concentrated in red blood cells and subsequently distributed to other organs (highest concentrations in liver, lung, kidney, and spleen), followed by urinary excretion. Whole body autoradiography following intravenous injection of either arsenite or arsenate into mice and hamsters illustrates this distribution. There is also a significant accumulation of arsenate in the skeleton, presumably by exchange with phosphate (Lindgren et al., 1983). The same distribution pattern applies to inhaled arsine. Application of pentavalent arsenic to skin results first in an accumulation of arsenic in the skin, followed by distribution to other organs, followed by urinary excretion. Significant deposition in hair and nails has been demonstrated in man and animals.

Metabolism and excretion: The pathways of arsenic metabolism vary with the type of arsenic compound administered, route of administration, and animal species. Some aspects have been reviewed (Klevay, 1976; Odanaka et al., 1980; Peoples, 1983). Biotransformation of arsenite to arsenate occurs in the mouse (this is probably a detoxication mechanism) while the reverse reaction has been observed in dogs (Tsukamoto, 1983). Urinary and fecal excretion products are inorganic arsenic and the result of successive methylation to MAA and DMA (for structures see B, above) in most species including man (Buchet et al., 1981; Bertolero et al., 1981; Marafante et al., 1985); however, there is no methylation in the marmoset monkey (Vahter et al., 1982), and the rat is an inappropriate species for studying arsenic metabolism since in this species nearly all of the administered arsenic is stored in red blood cells (Peoples, 1983).

Toxic effects: In general, arsenites are much more toxic than arsenates; the oral LD50 of arsenates in rats and mice is about 100 mg/kg and that of arsenites about 10 mg/kg; the acute oral LD50 of arsenic trioxide is 15 mg/kg in rats and 39 mg/kg in mice, and that of calcium arsenate is 812 mg/kg in rats. The LC50 of arsine by inhalation in mice has been estimated to be

0.67 mg/kg (0.5 mg/l) after 2-4 min; 3-10 ppm will produce symptoms in man after several hours of exposure. The intraperitoneal LD50 in mice is about 2.5 mg/kg in several strains.

Acute and chronic effects of arsenic intoxication in man have been summarized (Landrigan, 1981; IARC, 1980; Arena and Drew, 1986). They include a burning sensation of mouth and throat; metallic, garlicky odor of breath and feces; difficulty in swallowing; vomiting; diarrhea; and cyanosis. Chronic effects include hyperpigmentation and keratosis (characteristics of prolonged treatment with Fowler's solution), vascular effects ("blackfoot disease"), cirrhosis of the liver, and effects on the hematopoietic system (leukopenia, anemia). The chief toxic effect of inhaled arsine is due to its binding to hemoglobin, resulting in extensive hemolysis and hematuria followed by jaundice; the usual cause of death is renal failure.

Carcinogenic effects: As late as 1980 it was believed that arsenic compounds were not carcinogenic in experimental animals, and this conclusion was drawn from a summary of largely negative results (IARC, 1980). Since that time evidence has appeared which indicates carcinogenicity in rats (Ivankovic et al., 1979), mice (Rudnai and Börzsönyi, 1980), and Syrian golden hamsters (Ishinishi et al., 1983; Yamamoto et al., 1987). While some of these experiments may be questioned on the basis of inadequate controls or low though statistically significant incidence of tumors, the previous position can no longer be justified.

The evidence for carcinogenicity of arsenic compounds in man is more positive, and this has been reviewed (Landrigan, 1981; IARC, 1980, 1982; Furst, 1983). A correlation was established between the appearance of skin cancer and arsenic concentration in the well water in certain regions of Taiwan (Tseng, 1977). Skin cancers were also noted repeatedly in patients after prolonged treatment with Fowler's solution (potassium arsenite) and in vineyard workers employing arsenical pesticides. Lung cancers have been noted in men involved in the production of arsenicals (Mabuchi et al., 1980). Other studies (involving workers in copper smelters and mines) are not as clear-cut since exposure to other materials occurred concomitantly. There is still an open question whether arsenic compounds are primary carcinogens or co-carcinogens, but the bulk of the evidence is in favor of the former.

Mutagenic and teratogenic effects: Sodium arsenite and arsenate are not mutagenic in the Ames test or in E. coli (Sunderman, 1984) but are weakly positive in B. subtilis. Both are strongly teratogenic in the hamster (Ferm and Hanlon, 1985; Hanlon and Ferm, 1986a, 1986b) and in the mouse (Baxley et al., 1981).

G. Emergency Treatment

The treatment of poisoning by arsenic compounds, including use of BAL therapy, has been discussed (Arena and Drew, 1986).

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with dilute boric acid solution followed by water. Since some arsenic compounds are readily absorbed through the skin, avoid rubbing of skin or increasing its temperature. For eye exposure, irrigate immediately with dilute boric acid solution followed by copious quantities of running water for at least 15 minutes. Obtain ophthalmological evaluation.

2. Ingestion: Induce vomiting. Refer for gastric lavage.

3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.

4. Refer to physician at once. Consider treatment for pulmonary irritation.

H. References

ACGIH. 1987. Threshold Limit Values and Biological Exposure Indices for 1987-1988. American Conference of Governmental Industrial Hygienists, Cincinnati, OH.

Aggett, J. and R. Kadwani. 1983. Anion-exchange method for speciation of arsenic and its application to some environmental analyses. Analyst 108:1495-1499.

Arena, J.M. and R.H. Drew (eds). 1986. Poisoning, 5th ed. Charles C. Thomas, Springfield, IL.

Baxley, M.N., R.D. Hood, G.C. Vedel, W.P. Harrison, and G.M. Szczech. 1981. Prenatal toxicity of orally administered sodium arsenite in mice. Bull Environ Contam Toxicol 26:749-756.

Bertolero, F., E. Marafante, J.E. Rade, R. Pietra, and E. Sabbioni. 1981. Biotransformation and intracellular binding of arsenic in tissues of rabbits after intraperitoneal administration of ^{74}As labelled arsenite. Toxicology 20:35-44.

Brooks, R.R., D.E. Ryan, and H. Zhang. 1981. Atomic absorption spectrometry and other instrumental methods for quantitative measurement of arsenic. Anal Chim Acta 131:1-16.

Buchet, J.P., R. Lauwerys, and H. Roels. 1981. Comparison of the urinary excretion of arsenic metabolites after a single oral dose of sodium arsenite, monomethyl arsonate, or dimethylarsinate in man. Int Arch Occup Environ Health 48:71-79.

Burke, R.W. and B.I. Diamondstone. 1977. Procedures for the determination of arsenic, copper and nickel by molecular absorption spectrometry. in Procedures Used at the National Bureau of Standards to Determine Selected Trace Elements in Biological and Botanical Materials. Pages 73-79 Mavrodineanu, R. (ed). U.S. Dept. of Commerce, National Bureau of Standards, Washington, DC.

Chana, B.S. and N.J. Smith. 1987. Urinary arsenic speciation by high-performance liquid chromatography/atomic absorption spectrometry for monitoring occupational exposure to inorganic arsenic. Anal Chim Acta 197:177-186.

Cox, D.H. 1980. Arsine evolution--electrothermal atomic absorption method for the determination of nanogram levels of total arsenic in urine and water. J Anal Toxicol 4:207-211.

Ferm, V.H. and D.P. Hanlon. 1985. Constant rate exposure of pregnant hamsters to arsenate during early gestation. Environ Res 37:425-432.

Fowler, B.A. (ed). 1983. Biological and Environmental Effects of Arsenic. Elsevier, NY.

Furst, A. 1983. A new look at arsenic carcinogenesis. in Lederer, W.H. and R.J. Fensterheim (loc. cit.), pp. 151-164.

Hanlon, D.P. and V.H. Ferm. 1986a. Concentration and chemical status of arsenic in the blood of pregnant hamsters during critical embryogenesis. I. Subchronic exposure to arsenate utilizing constant rate administration. Environ Res 40:372-379.

Hanlon, D.P. and V.H. Ferm. 1986b. Concentration and chemical status of arsenic in the blood of pregnant hamsters during critical embryogenesis. II. Acute exposure. Environ Res 40:380-390.

IARC, International Agency for Research on Cancer. 1980. in Some Metals and Metallic Compounds, IARC Monograph 23. Pages 39-141 Lyon, France.

IARC, International Agency for Research on Cancer. 1982. Monograph Supplement 4. Lyon, France.

IARC, International Agency for Research on Cancer. 1986. IARC Scientific Publications 71: Environmental Carcinogens. Selected Methods of Analysis, Vol. 8. Lyon, France.

Ishinishi, N.A., A. Yamamoto, A., A. Hisanaga, and T. Inamasu. 1983. Tumorigenicity of arsenic trioxide to the lung in Syrian golden hamsters by intermittent instillations. Cancer Lett 21:141-147.

Ivankovic, S., G. Eisenbrand, and R. Preussmann. 1979. Lung carcinoma induction in BD rats after a single intratracheal instillation of an arsenic-containing pesticide mixture formerly used in vineyards. Int J Cancer 24:786-788.

Kang, H.K. and J.L. Valentine. 1977. Acid interference in the determination of arsenic by atomic absorption spectrometry. Anal Chem 49:1829-1832.

Klevay, L.M. 1976. Pharmacology and toxicology of heavy metals: Arsenic. Pharmacol Ther A 1:189-209.

Krynitsky, A.J. 1987. Preparation of biological tissue for determination of arsenic and selenium by graphite furnace atomic absorption spectrometry. Anal Chem 59:1884-1886.

Landrigan, P.J. 1981. Arsenic -- state of the art. Am J Industr Med 2:5-14.

Lederer, W.H. and R.J. Fensterheim (eds). 1983. Arsenic -- Industrial, Biomedical, Environmental Perspectives. Proc Arsenic Symposium, Gaithersburg, MD. Van Nostrand Reinhold Co., NY.

Lewis, R.G. 1977. Determination of arsenic and arsenicals in foods and other biological materials. Residue Revs 68:123-149.

Lindgren, A., M. Vahter, and L. Dencker. 1983. Autoradiographic studies on the distribution of arsenic in mice and hamsters administered ^{74}As-arsenite or -arsenate. Acta Pharmacol Toxicol 51:253-265.

Mabuchi, K., A.M. Lilienfeld, and L.M. Snell. 1980. Cancer and occupational exposure to arsenic: a study of pesticide workers. Prev Med 9:51-77.

Maitani, T., S. Uchiyama, and Y. Saito. 1987. Hydride generation -- flame atomic-absorption spectrometry as an arsenic detector for high-performance liquid chromatography. J Chromatog 391:161-168.

Marafante, E., M. Vahter, and J. Envall. 1985. The role of methylation in the detoxication of arsenate in the rabbit. Chem-Biol Interactions 56:225-238.

Morita, M., T. Uehiro, and K. Fuwa. 1981. Determination of arsenic compounds in biological samples by liquid chromatography with inductively coupled argon plasma-atomic emission spectrometric detection. Anal Chem 53:1806-1808.

NIOSH. 1977. NIOSH Manual of Analytical Methods, 2nd ed. U.S. Dept. of Health, Education and Welfare, NIOSH, Cincinnati, OH.

Odanaka, Y., O. Matano, and S. Gato. 1980. Biomethylation of inorganic arsenic by the rat and some laboratory animals. Bull Environ Contam Toxicol 24:452-459.

Peoples, S.A. 1983. The metabolism of arsenic in man and animals. in Lederer, W.H. and R.J. Fensterheim (loc. cit.), pp. 126-133.

Reay, P.F. and C.J. Asher. 1977. Preparation and purification of ^{74}As-labelled arsenate and arsenite for use in biological experiments. Anal Biochem 78:557-560.

Ricci, G.R., L.S. Shepard, G. Colovos, and N.E. Hester. 1981. Ion chromatography with atomic absorption spectrometric detection for determination of organic and inorganic arsenic species. Anal Chem 53:610-613.

Rudnai, P. and M. Börzsönyi. 1980. Carcinogenic effect of arsenic trioxide in transplacentally and neonatally treated CFL mice. Nat Sci 2:11-18, Chem Abstr 95:198782j.

Sittig, M. 1985. Handbook of Toxic and Hazardous Chemicals and Carcinogens. 2nd ed. Noyes Data Corp., Park Ridge, NJ.

Snyder, C.A. and D.A. Isola. 1979. Assay for arsenic trioxide in air. Anal Chem 51:1478-1480.

Sunderman, F.W., Jr. 1984. Recent advances in metal carcinogenesis. Ann Clin Lab Sci 14:93-122.

Tseng, W-P. 1977. Effects and dose-response relationships of skin cancer and blackfoot disease with arsenic. Environ Health Perspect 19:109-119.

Tsukamoto, H. 1983. Metabolism and renal handling of sodium arsenate in dogs. Am J Vet Res 44:2331-2335.

Uthus, E.D., M.E. Collings, W.E. Cornatzer, and F.H. Nielsen. 1981. Determination of total arsenic in biological samples by arsine generation and atomic absorption spectrometry. Anal Chem 53:2221-2224.

Vahter, M., E. Marafante, A. Lindgren, and L. Dencker. 1982. Tissue distribution and subcellular binding of arsenic in marmoset monkeys after injection of ^{74}As-arsenite. Arch Toxicol 51:65-77.

Vahter, M. and H. Norin. 1980. Metabolism of ^{74}As-labeled trivalent and pentavalent inorganic arsenic in mice. Environ Res 21:446-457.

Weast, R.C. (ed). 1979. CRC Handbook of Chemistry and Physics, 60th ed., CRC Press Inc., Boca Raton, FL.

Yamamoto, A., A. Hisanaga, and N. Ishinishi. 1987. Tumorigenicity of inorganic arsenic compounds following intratracheal instillations to the lungs of hamsters. Int J Cancer 40:220-223.